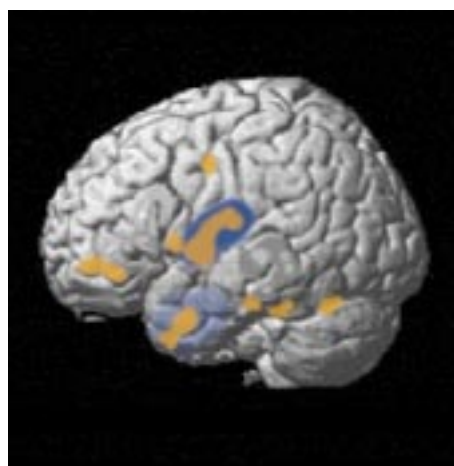


## Graphic Evidence

### Brain Activity During Cue-Induced Craving

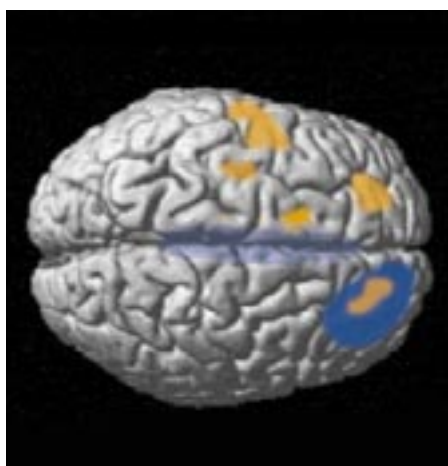
In these extraordinary images, Dr. Katherine Bonson and her colleagues at NIDA's Intramural Research Program have captured the process of a cocaine-related cue triggering craving for cocaine in the brain of an addicted individual. The investigators used positron emission tomography (PET) to create images of brain activity in 11 cocaine-addicted volunteers who reported on the intensity of their craving for cocaine while watching videotapes showing drug paraphernalia. In the three views of the human brain shown below, yellow patches indicate areas where increased activation corresponded to reports of increased craving when the videotape showed drug-related images. Blue overlays mark the key brain structures in which these areas of increased activation occurred; taken together, as explained below, they form a coordinated network that integrates memory, emotion, attention, and expectation into a desire to use cocaine.



**A. Left side view**

The **amygdala** and **rhinal cortex** (A, light blue) are involved in identifying familiar objects and assigning them a motivational value. In cocaine craving, the amygdala and rhinal cortex appear to link a perceived object—in this case, video representations of drug paraphernalia—with cocaine and with the memory of experiences with both the object and the drug.

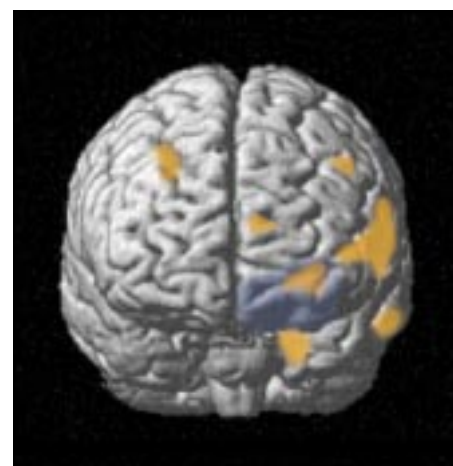
The **insula** (dark blue), which shares connections with the rhinal cortex, helps confirm the association of perception and memory. In individuals addicted to cocaine, the insula appears to “authorize” the assignment of emotional significance to the link between the perceived cue and memories of the physical response to the drug.



**B. Top view (front brain to the right)**

The **anterior cingulate** (B, light blue) acts to establish and process emotional memory and to control allocation of attention. It links perceived cues with emotional states in which the expectation of a particular outcome has repeatedly been fulfilled. In cocaine addiction, the anterior cingulate stimulates the recall of specific feelings associated with drug use, “reminding” an individual of repeated drug reward.

Increased activity in the amygdala, rhinal cortex, insula, and anterior cingulate appears to initiate the process that leads to craving by linking visual cues to memory. This complex process is monitored by the dorsolateral prefrontal cortex (B, dark blue), a brain region that acts as a “manager” for working memory. In cocaine addiction, this region maintains the brain’s focus on cocaine-related cues and produces an active urge to take the drug.



**C. Front view**

The **orbitofrontal cortex** (C, light blue) helps to form, and then maintain or modify, expectations of possible outcomes by combining memories of past experiences with changing current events. In cocaine craving, the orbitofrontal cortex appears to guide addicted individuals away from decisions based on objective consideration of the negative effects of drug use—its risks to personal, social, and professional life—and toward acting on an emotion-based expectation of outcome or reward.

**Source:** Bonson, K.L., et al., 2002. Neural systems and cue-induced cocaine craving. *Neuropsychopharmacology* 26(3):376-386.